REMARKS

Claims 1 and 2 are pending in the application.

I. Priority

At paragraph 2 of the Office Action, the Examiner states that the U.S. PTO will not recognize Applicants' claim to priority of U.S. provisional application number 60/073,763 (filed February 5, 1998) for the reasons set forth in the Action. The Examiner further states that the earliest priority date for the instant application is February 5, 1999, the filing date of parent application number 09/245,808.

Applicants respectfully traverse the Examiner's position for the following reasons.

Applicants note that the Examiner's position is based on an allegation of lack of priority entitlement for the subject matter relating to the amino acid sequence of the Breast Cancer Resistance Protein (BCRP), SEQ ID NO:1, of the pending application. Applicants respectfully submit that all of the objections based on this issue are unfounded as the correct amino acid sequence for BCRP, as set forth in SEQ ID NO:1, is clearly supported and enabled in the provisional application (60/073,763) from which priority is claimed and thus the subject matter of claims 1 and 2 is entitled to priority.

The Examiner notes that the provisional application refers to a polypeptide of 663 amino acids while the pending application refers to a polypeptide having the sequence of SEQ ID NO:1 which has 655 amino acids. However, it is submitted that one skilled in the art would have readily found the provisional application to provide adequate support and enablement for the 655 amino acid sequence of SEQ ID NO:1 of the pending application by at least the recitation of the corresponding open reading frame (ORF), as discussed in more detail below. Even more, it would have been clear to the skilled artisan that the first eight amino acids appearing in the deduced polypeptide sequence in the provisional application were an obvious error and that the BCRP protein disclosed in the provisional application corresponds to the 655 amino acid polypeptide disclosed in the pending application.

Applicants note that in order to properly claim benefit of a provisional application, the provisional application must adequately support and enable the subject matter claimed in the non-provisional application (*New Railhead Mfg., LLC v. Vermeer Mfg. Co.*, 298 F.3d 1290, 63 USPQ2d 1843 (Fed. Cir. 2002). Applicants assert that this burden is clearly met in the provisional application and that, for the following reasons, the 655 amino acid sequence of the pending application is adequately supported and enabled by the provisional application. In particular, page 21, lines 17-22, of the provisional application specifically states that Applicants sequenced a 2418 bp nucleic acid molecule, and that further analysis revealed an ORF that began at position 239 and ended with the stop codon TAA at position 2204-6. This yields an ORF consisting of 1965 nucleotides (nucleotides 239 to 2203), which encodes 655 amino acids. The encoding sequence from which this ORF may be translated is provided in Figure 2C of the priority document. Indeed the translation of this region which provides 655 amino acids is disclosed in the provisional application in Figure 2A. Thus the 655 amino acid sequence as disclosed in the pending application is explicitly disclosed as an entity in the provisional application and thus is adequately supported and enabled by the provisional application.

Furthermore, not only is the ORF which provides the correct sequence adequately supported and enabled by the provisional application, the skilled artisan would have been aware that the polypeptide sequence provided in Figure 2A erroneously contains an additional eight N-terminal amino acids. It is submitted that one skilled in the art armed with common general knowledge would have realized that the erroneous 8-mer at the beginning of the amino acid sequence should be ignored.

The fact that the 8-mer is in error is evident for at least two reasons. Firstly, the provisional application specifically refers to an ORF which, when translated, provides a 655 amino acid sequence. Furthermore, the referred-to ORF starts with an ATG codon, which codes for methionine, whereas the erroneous 663 amino acid sequence does not start with methionine. This would alert one of ordinary skill in the art to an obvious error. Secondly, the first amino acid in eukaryotic translated proteins is, almost without exception, methionine; thus one skilled in the art would realize that the first methionine residue is in fact the correct starting point for the polypeptide and that the preceding eight amino acids are recited in error.

In further support of the obvious nature of the error in the polypeptide sequence disclosed by the priority application, Sherman et al. (*Biochmica et Biophysica Acta*, 609 (1980) 343-346) is submitted herewith. Sherman et al. indicate that eukaryotic genes "use solely AUG codons for initiating translation" (see, for example, page 343, first paragraph after the Summary; page 345, last paragraph; and page 346, paragraph 1). In particular, on page 344 in the third and fourth lines after Table 1 it is stated that the codon GCU (amongst others, which is GCT in DNA) can be eliminated as a functional equivalent (i.e. capable of initiating translation) to AUG. GCT is the codon that "encodes" the first residue (alanine) of the 663 amino acid sequence recited in Figure 2A of the priority document. As the GCT codon is not known to be an initiation codon, a polypeptide sequence starting with an amino acid encoded by this codon is clearly incorrect.

This is further supported by the enclosed extract from the textbook "Biochemistry" by Lubert Stryer, which states at point 3 of page 904 that "[t]he initiating codon in eukaryotes is always AUG." AUG is the rnRNA codon that codes for methionine with the corresponding DNA sequence being ATG. The presence of the alanine in the first position of the amino acid sequence of Figure 2A of the priority application and its encoding sequence would therefore have alerted the reader to an error in the amino acid sequence for the ORF as shown in Figure 2A. Once the skilled artisan reviewed the discussion at pages 21-22 of the provisional application, where it is stated that translation begins at position 239 of the polynucleotide of Figure 2C, it would have been readily apparent that the first eight residues shown in Figure 2A were included in error.

In summary, the ORF corresponding to the protein sequence of BCRP (i.e., SEQ ID NO: 1) was disclosed and taught in the priority application. The ORF for BCRP was determined after analysis of start and stop codons revealed "the presence of a long ORF that began at position 239, and ended with the stop codon TAA at position 2204-6" (see provisional application at page 21). The codon starting at position 239 is ATG, which indicates that the start codon used to determine the ORF was ATG which encodes methionine. Inherent to this process is that the protein of interest will start with the amino acid methionine. Since the protein sequence recited in Figure 2A of the priority document does not begin with a methionine a person skilled in the art would have determined that this sequence includes an obvious error. With this in mind, a person

skilled in the art would have turned to the more detailed description in the provisional application to determine the protein sequence of BCRP. In light of the recitation of the ORF and since a codon consists of three nucleic acids, it would have been directly and unambiguously determined by a person skilled in the art that the recited ORF corresponds to a protein that is 655 amino acids in length. Next, a person skilled in the art would have confirmed the ORF recited in the priority document translates into the same amino acid sequence as that of the 655 amino acid sequence of SEQ ID NO:1. To this end, a person skilled in the art would have used a software program, or manually performed the same, to translate the ORF and compare that sequence to the amino acid sequence of SEQ ID NO:1. Alternatively, a person skilled in the art would have performed a pair-wise sequence alignment of the polynucleotide corresponding to the ORF and the amino acid sequence of SEQ ID NO:1.

In support of this, Dr. Willard Freeman, a scientist unrelated to the inventors, was asked to determine whether the sequence provided in SEQ ID NO:1 was disclosed and taught in the provisional application. As reported in his Declaration[1] submitted herewith, he was able to directly and unambiguously demonstrate that a person skilled in the art would indeed derive the sequence disclosed in SEQ ID NO: 1 from the priority document on the basis of information provided in the provisional application (i.e., the ORF at page 21). Furthermore, Dr Freeman is of the view that the 663 amino acid polypeptide sequence in the provisional application is clearly an error and that the correct sequence is obvious, namely the 655 amino acid sequence as set forth in SEQ ID No. 1. The Freeman Declaration supports the fact that one skilled in the art would have been able to derive the polypeptide of SEQ ID NO:1 from the priority application using common general knowledge, and that the inclusion of the eight N-terminal amino acids is an error and that the correction of that error is obvious, i.e. in line with the disclosure of the ORF that those eight amino acids should be removed.

In addition to the comments above on the entitlement of the sequence disclosed in SEQ ID NO:1 to priority, Applicants also respectfully assert that the priority considerations do not apply to claims 1 and 2 in the first place. Applicants submit that claims 1 and 2 do not rely on

[1] The Freeman Declaration was submitted in the European Opposition to European Patent No. 1054894, which is the European counterpart to the instant U.S. application.

SEQ ID NO:1 being entitled to priority to achieve priority. Their entitlement to priority is independent of any findings in relation to the priority of the SEQ ID NO:1 sequence.

In particular, Applicants note that claims 1 and 2 concern antibodies that bind the polypeptide of SEQ ID NO:1. Even if antibodies to the polypeptide consisting of 663 amino acids alone were considered to be entitled to priority, this polypeptide wholly includes the 655 amino acid sequence of the pending application and hence includes all the epitopes derivable from that shorter sequence. As a consequence, all the antibodies claimed in claim 1 are disclosed in the priority application, independent of the finding on whether or not the sequence as set forth in SEQ ID NO:1 itself is entitled to priority. Similar comments apply to claim 2 which is directed to the use the antibodies of claim 1.

In summary, for the reasons set forth above Applicants respectfully assert that the provisional application adequately supports and enables the 655 amino acid polypeptide of SEQ ID NO:1 of the pending application. Moreover, claims 1 and 2 are adequately supported and enabled by the provisional application regardless of whether the 655 amino acid polypeptide of SEQ ID NO:1 is supported by the provisional application as they will bind to the 655 amino acid polypeptide encompassed wholly within the larger 663 amino acid polypeptide of the provisional application. In view thereof, Applicants respectfully request reconsideration and acknowledgment that the pending application is entitled to the February 5, 1998 priority date of the provisional application.

II. Rejection Under 35 U.S.C. §103

A. At paragraph 3 of the Office Action, claims 1 and 2 are rejected under 35 U.S.C. §103, as being obvious over Allikmets (Can. Res., 1998) in view of Campbell (1984).

In response, Applicants reiterate their position that the pending application is properly entitled to the priority filing date of February 5, 1998 of U.S. provisional application number 60/073,763 for the reasons set forth above. As such, Allikmets may not serve as legally effective prior art against the pending claims. Furthermore, Campbell does not teach or suggest the subject matter of the pending claims. Therefore, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

B. At paragraph 4 of the Office Action, claims 1 and 2 are rejected under 35 U.S.C. §103, as being obvious over GenBank Accession No. AAC97367 (12/12/1998) in view of Campbell (1984).

In response, Applicants reiterate their position that the pending application is properly entitled to the priority filing date of February 5, 1998 of U.S. provisional application number 60/073,763 for the reasons set forth above. As such, GenBank Accession No. AAC97367 may not serve as legally effective prior art against the pending claims. Furthermore, Campbell does not teach or suggest the subject matter of the pending claims. Therefore, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

III. Conclusion

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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